

NON-TECHNICAL ABSTRACT:

"A Phase I/II Study of an Anti-tumor Vaccination Using $\alpha(1,3)$ Galactosyltransferase Expressing Allogeneic Tumor Cells in Patients with Refractory or Recurrent Melanoma Cancer."

Unfortunately, despite the best clinical efforts and breakthroughs in biotechnology, most patients diagnosed with advanced stage melanoma continue to die from their disease. Reasons for this include that: 1) patients are often diagnosed at a time when their melanoma has already spread to other sites such as the chest cavity, bone, liver, and brain limiting the options for surgical excision. and 2) the cancer cells are resistant or become resistant to chemotherapy drugs used to treat the patient. Resistance to one type of chemotherapy agent often rapidly leads to resistance against many other chemotherapy drugs.

These reasons are the major causes of cancer progression that are usually discussed when considering treatment options for patients with disease that continues to grow and spread. However, another important part of the body should be considered-- the immune system. Scientists have clearly shown that melanoma cancer cells produce a number of abnormal proteins or abnormal amounts of certain proteins found in normal melanoma cells. Normally one would expect a patient to develop an immune response against these abnormal proteins found in their cancer and attack them much the way we would fight off an infection from a foreign bacteria or virus. However, for reasons that scientists do not fully understand, the immune system fails to respond to these abnormal proteins and does not attack the melanoma cancer cells. This human clinical trial proposes a new way to make the immune system recognize the cancer and encourage it to attack the cancer cells.

Many people are familiar with the idea of transplants between people of organs like the kidneys or heart. When an organ transplant between two people is completed one of the problems that can occur is rejection of the donated organ by the recipient. This can occur because the immune system of the patient who receives the organ attacks the donated organ. If you were to attempt to transplant a pig heart to a human the rejection would be dramatically stronger than when organs are transplanted between two people. This is partly because lower animals express sugar-protein patterns on the surface of their cells that humans do not. In fact, our immune systems can quickly recognize tissues from lower mammals such as the pig or the mouse and destroys them.

In this project, we have put a mouse gene into human melanoma cancer cells that produces these abnormal sugar patterns and stimulates the immune system to attack the melanoma cancer. This strategy works well to kill human other cancer cells in the laboratory, but it needs to be tried in melanoma cancer patients to see if it will be effective and to determine if such a treatment causes any side effects. We propose to test this new treatment in patients with melanoma cancer who have failed at least one type of chemotherapy treatment to see if it can stop, slow or destroy tumors in these patients. Patients will be injected with an anti-tumor vaccine consisting of a mixture of three types of dead human melanoma cancer cells that have been genetically altered to express the mouse gene responsible for making this abnormal sugar-protein on the cells. This trial is scientifically designed and conducted in an ethical manner.